

Attorney Docket No.: BDA-0038
Inventors: Roger S. Cubicciotti
Serial No.: 09/171,885
Filing Date: October 28, 1998
Page 2

(b) a selected drug specifically bound to the synthetic receptor via a saturable, noncovalent interaction between the selected drug and the synthetic receptor that can be competitively inhibited by structural analogs of the selected drug, wherein the selected drug is specifically bound to the synthetic receptor with lower affinity than to the drug's pathophysiologic receptor so that the selected drug preferentially binds to the pathophysiologic receptor with no loss of efficacy of the selected drug; and

*E1
cancelled*
(c) a biologic or biocompatible structure to which the selected synthetic receptor or selected drug is immobilized.

14. (amended) A prodrug complex comprising a drug specifically bound to a synthetic receptor selected to bind to said drug via a saturable, noncovalent interaction between the selected drug and the synthetic receptor that can be competitively inhibited by structural analogs of the selected drug, wherein said synthetic receptor is selected by a method selected from the group consisting of combinatorial selection, monoclonal antibody selection and antibody engineering, wherein said drug preferentially dissociates from the synthetic receptor and binds to a pathophysiologic receptor following administration of the prodrug complex to an organism.

Attorney Docket No.: BDA-0038
Inventors: Roger S. Cubicciotti
Serial No.: 09/171,885
Filing Date: October 28, 1998
Page 3

16. (amended) A method of producing a prodrug complex comprising:

(a) selecting a drug to be delivered as a prodrug complex;

E2
(b) selecting a synthetic receptor that specifically binds to the drug via a saturable, noncovalent interaction between the selected drug and the synthetic receptor that can be competitively inhibited by structural analogs of the selected drug, wherein said synthetic receptor is selected by at least one of combinatorial selection, screening and selection of antibodies, engineered antibodies, oligonucleotides or oligosaccharides, or in vitro evolution; and

(c) specifically binding the selected drug to the selected synthetic receptor to form a prodrug complex.

E3
18. (amended) A multi-prodrug complex comprising at least two drugs specifically bound to at least two synthetic receptors via a saturable, noncovalent interaction between the drugs and the synthetic receptors that can be competitively inhibited by structural analogs of the drugs, wherein at least one of the synthetic receptors specifically bound to said drug is selected by

Attorney Docket No.: BDA-0038
Inventors: Roger S. Cubicciotti
Serial No.: 09/171,885
Filing Date: October 28, 1998
Page 4

E3
cancel
a method selected from the group consisting of combinatorial selection, monoclonal antibody selection and antibody engineering, and wherein said drugs preferentially dissociate from the synthetic receptors and bind to pathophysiologic receptors following administration of the multi-prodrug complex to an organism.

20. (amended) A method of producing a multi-prodrug complex comprising:

(a) selecting at least two drugs to be delivered as a multi-prodrug complex;

E4
(b) selecting at least two synthetic receptors that specifically bind to the selected drugs via a saturable, noncovalent interaction between the selected drug and the synthetic receptor that can be competitively inhibited by structural analogs of the selected drug, wherein at least one of the synthetic receptors is selected by at least one of combinatorial selection, screening and selection of antibodies, engineered antibodies, oligonucleotides or oligosaccharides, or in vitro evolution; and

(c) specifically binding the selected drugs to the selected synthetic receptors to form a multi-prodrug complex.

Attorney Docket No.: BDA-0038
Inventors: Roger S. Cubicciotti
Serial No.: 09/171,885
Filing Date: October 28, 1998
Page 5

22. (amended) A prodrug complex comprising:

ES (a) a synthetic receptor selected from the group consisting of drug receptors, transmitter receptors, autocoid receptors, cytokine receptors, antibodies, antibody fragments, molecular recognition units, engineered antibodies, antibody mimics, adhesion molecules, agglutinins, integrins, selectins, nucleic acids and biopolymers comprising nucleotides, saccharides, fatty acids, phenols, phosphates, sulfates, other organic monomers or nonbiologic monomers, wherein said synthetic receptor is selected by at least one of combinatorial selection, screening and selection of antibodies, engineered antibodies, oligonucleotides or oligosaccharides, or in vitro evolution; and

(b) a selected drug specifically bound to the synthetic receptor via a saturable, noncovalent interaction between the selected drug and the synthetic receptor that can be competitively inhibited by structural analogs of the selected drug, wherein the selected drug is specifically bound to the synthetic receptor with lower affinity than to the drug's pathophysiologic receptor so that the selected drug dissociates from the synthetic receptor and preferentially binds to the pathophysiologic receptor.

Attorney Docket No.: BDA-0038
Inventors: Roger S. Cubicciotti
Serial No.: 09/171,885
Filing Date: October 28, 1998
Page 6

24. (amended) A method of enhancing delivery of a selected drug to a pathophysiologic receptor for said selected drug comprising:

36
(a) selecting a drug to be delivered as a prodrug complex and a synthetic receptor selected from the group consisting of drug receptors, transmitter receptors, autocoid receptors, cytokine receptors, antibodies, antibody fragments, molecular recognition units, engineered antibodies, antibody mimics, adhesion molecules, agglutinins, integrins, selectins, nucleic acids and biopolymers comprising nucleotides, saccharides, fatty acids, phenols, phosphates, sulfates, other organic monomers or nonbiologic monomers, wherein said synthetic receptor is selected by at least one of combinatorial selection, screening and selection of antibodies, engineered antibodies, oligonucleotides or oligosaccharides, or in vitro evolution, and wherein said selected drug binds to the selected synthetic receptor with lower affinity than to the drug's pathophysiologic receptor;

(b) specifically binding the selected drug to the selected synthetic receptor so that a prodrug complex is produced, said prodrug complex comprising the selected drug and the selected synthetic receptor specifically bound via a saturable, noncovalent interaction between the selected drug and the synthetic receptor

Attorney Docket No.: BDA-0038
Inventors: Roger S. Cubicciotti
Serial No.: 09/171,885
Filing Date: October 28, 1998
Page 7

*E6
concl.*
that can be competitively inhibited by structural analogs of the selected drug; and

(c) administering the prodrug complex to an organism so that the selected drug dissociates from the selected synthetic receptor and binds to the drug's pathophysiologic receptor.

26. (amended) A multi-prodrug complex comprising:

E7
(a) at least two synthetic receptors, at least one of which is selected from the group consisting of drug receptors, transmitter receptors, autocoid receptors, cytokine receptors, antibodies, antibody fragments, molecular recognition units, engineered antibodies, antibody mimics, adhesion molecules, agglutinins, integrins, selectins, nucleic acids and biopolymers comprising nucleotides, saccharides, fatty acids, phenols, phosphates, sulfates, other organic monomers or nonbiologic monomers, wherein said synthetic receptors are selected by at least one of combinatorial selection, screening and selection of antibodies, engineered antibodies, oligonucleotides or oligosaccharides, or in vitro evolution; and

(b) at least two selected drugs specifically bound to the synthetic receptors via a saturable, noncovalent interaction between the selected drugs and the synthetic receptors that can be

Attorney Docket No.: BDA-0038
Inventors: Roger S. Cubicciotti
Serial No.: 09/171,885
Filing Date: October 28, 1998
Page 8

E7
concluded

competitively inhibited by structural analogs of the selected drugs, wherein the selected drugs are specifically bound to the synthetic receptors with lower affinity than to the drugs' pathophysiologic receptors so that the selected drugs dissociate from the synthetic receptors and preferentially bind to their pathophysiologic receptors.

28. (amended) A method of enhancing delivery of selected drugs to pathophysiologic receptors for said selected drugs comprising:

E8

(a) selecting at least two drugs to be delivered as a multi-prodrug complex and at least two synthetic receptors, at least one of which is selected from the group consisting of drug receptors, transmitter receptors, autocoid receptors, cytokine receptors, antibodies, antibody fragments, molecular recognition units, engineered antibodies, antibody mimics, adhesion molecules, agglutinins, integrins, selectins, nucleic acids and biopolymers comprising nucleotides, saccharides, fatty acids, phenols, phosphates, sulfates, other organic monomers or nonbiologic monomers, wherein said synthetic receptors are selected by at least one of combinatorial selection, screening and selection of antibodies, engineered antibodies, oligonucleotides or